Clinical Approach to Snakebites and Envenomations

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Introduction – Snake Bites

- Over 3,000 species of snakes worldwide
  - Only 350 species are venomous
  - Even fewer cause significant human envenomations
- Cause more deaths than all other venomous animals

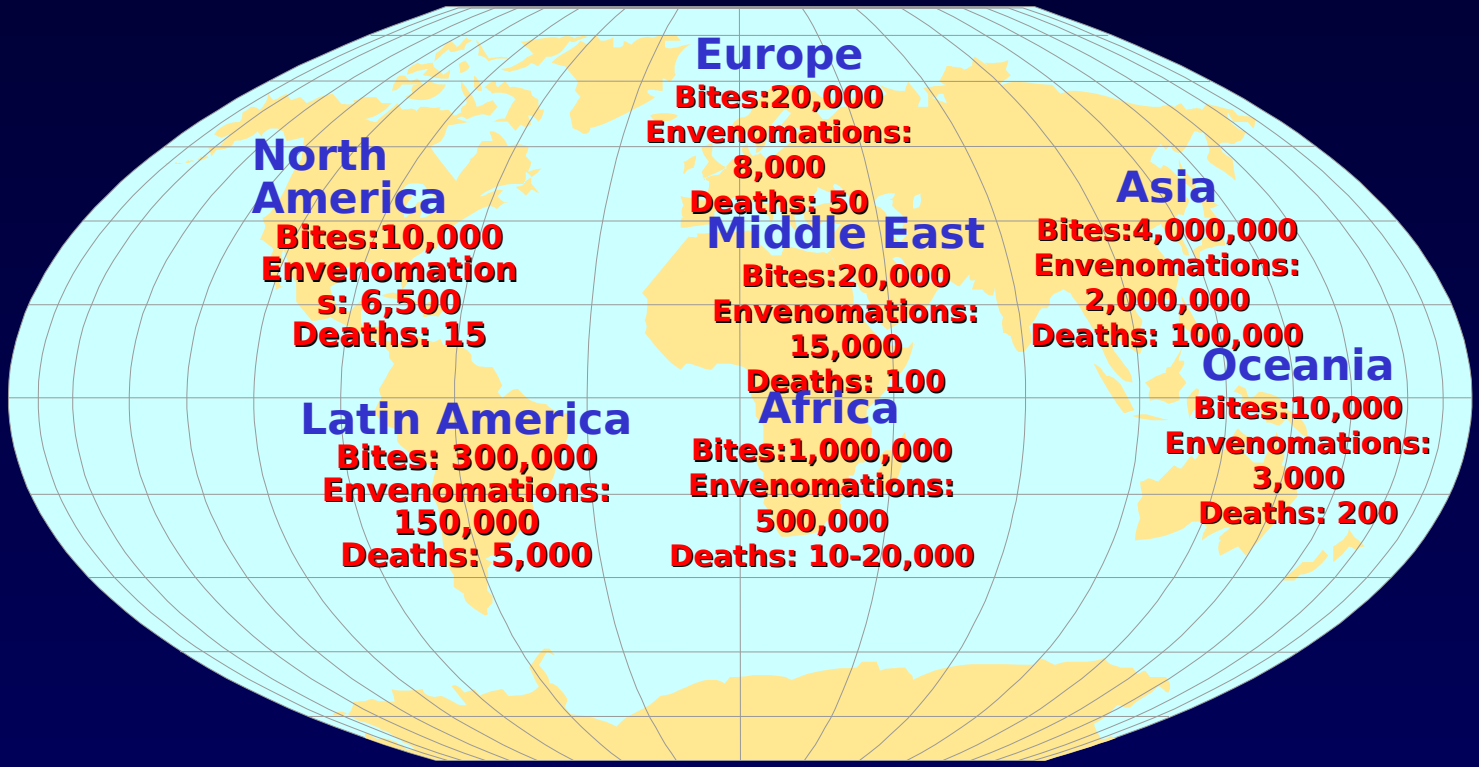
Introduction

- **Worldwide – 2.5 million envenomations/yr**
  125,000 deaths/yr
- **West African savanna – 23,000 deaths/yr**
- **Asia**
  - **78% hunter-gatherer tribes have antibodies to snake venom. Causes 5% of all deaths.**
  - **India – > 20,000 deaths/year (hospitalized)**
  - **Myanmar: snakebite is 7th most common cause of death**
- **United States – 10-15 deaths/yr**

Snake Envenomation - Difficulties

- **Dated literature (often > 40 yrs old)**
  - **Contradictory, varied data**
- **Limited epidemiology information**
  - **Majority of victims not hospitalized**
- **Biting snake species often not known**
- **Variable clinical presentations**

Figure 1. Estimated Snake Bites, Envenomations & Deaths



Worldwide

Bites: 5.4 million
Envenomations: 2.5 million Deaths: 125,000

Snakebite – Epidemiology

- **Most victims are residents of rural tropics**
- **Usually younger age (often children)**
- **Males >> Females**

Snakebite – U.S. Epidemiology

- 45,000 snakebites each yr
  - 8,000-10,000 bites by venous snakes per yr
  - 10-15 deaths per year
- 94% of bites occur in April to October
  - Most in July and August
  - Males 7x > Females

Snakebite – U.S. Epidemiology

Numbers of Bites per 100,000

North Carolina	18.8
Arkansas	17.2
Texas	14.7
Georgia	13.4
West Virginia	11.3
Mississippi	10.8
Louisiana	10.3
Oklahoma	8.9

Venomous Snakes

- **Viperidae**
  - **Subfamily viperinae (true vipers)**
  - **Subfamily crotalinae (folding fang)**
- **Elapidae (front-fanged)**
- **Hydrophidae (sea snakes)**
- **Colubridae (back-fanged)**
- **Atractaspidae (side-fanged)**

*Families in yellow responsible for the majority of worldwide envenomations

Venomous Snakes - Examples

- **Viperidae**
  - **Subfamily Viperinae: vipers, adders, asps**
  - **Subfamily Crotalinae: rattlesnakes, copperheads, cottonmouths, urutus, habus, fers-de-lance, bushmasters**
- **Elapidae: coral snakes, cobras, mambas, kraits, African garters**
- **Hydrophidae: sea snakes, sea kraits**
- **Colubridae: boomslangs, African bird snakes, vine snakes**
- **Atractaspidae: burrowing asps**

Venomous Snakes - USA

- **Pit Vipers (Crotalinae)**
  - **Rattlesnake (25 Crotalus sp.)**
  - **Pygmy rattlesnake (2 Sisturus sp.)**
  - **Copperhead (*Agkistrodon contortrix*)**
  - **Cottonmouth/water moccasin (*A. piscivorus*)**
- **Coral Snakes (Elapidae)**
  - **Eastern coral snake (*Micrurus fulvius*)**
  - **Arizona coral snake (*Micruroides euryxanthus*)**

Snakebite – Epidemiology U.S. and Canada

- 95% from Crotalids (pit vipers)
  - Rattlesnakes, cottonmouths, copperheads
- 2% from Elapids (coral snakes)
- 3% from exotic, foreign, or imported

Eastern Diamondback Rattlesnake

Crotalus adamanteus

Western Diamondback Rattlesnake

Crotalus atrox

Timber Rattler
Crotalus horridus

Pygmy Rattlesnake
Sisturus miliarius

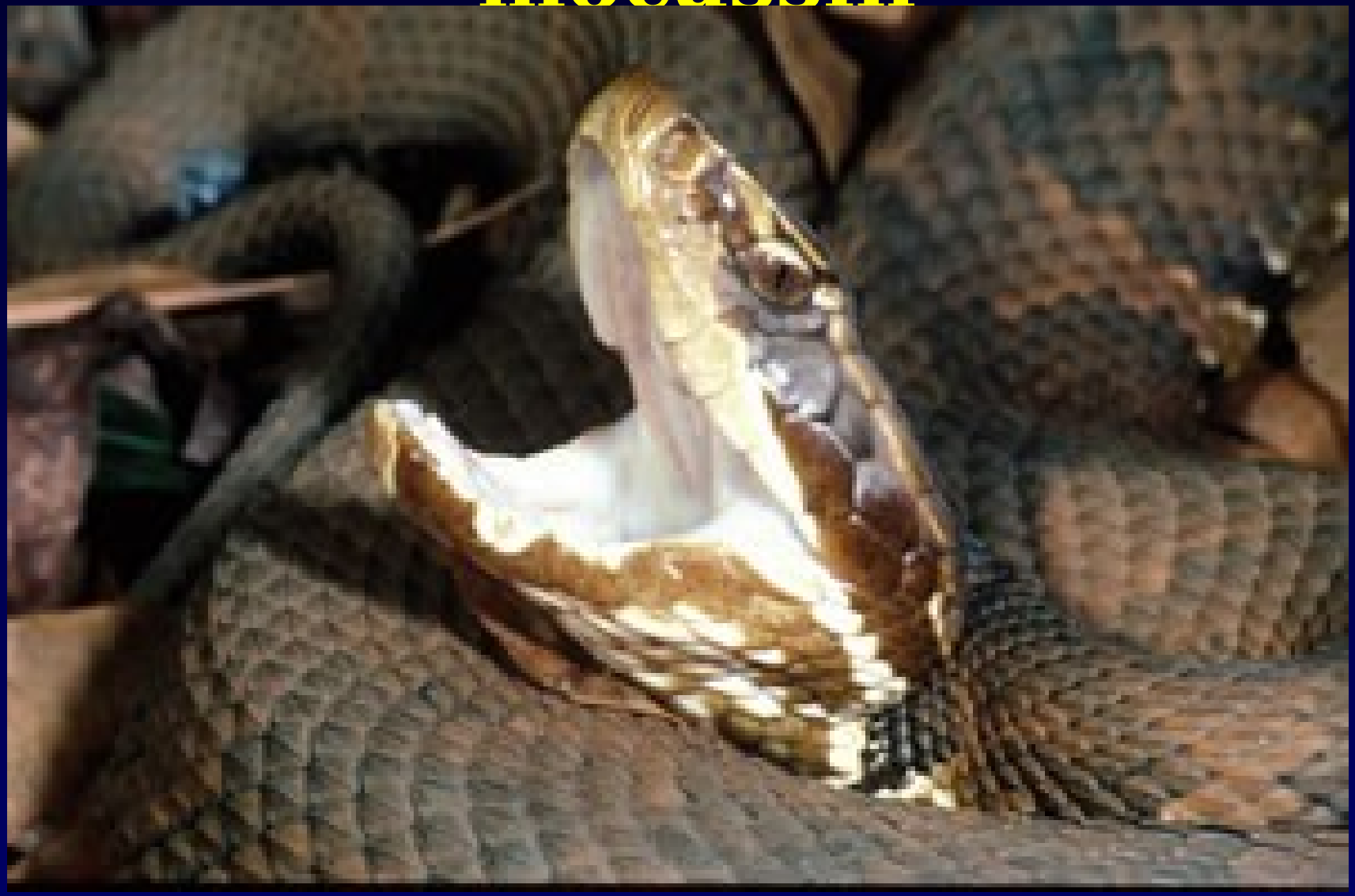
Copperhead

Agkistrodon contortrix

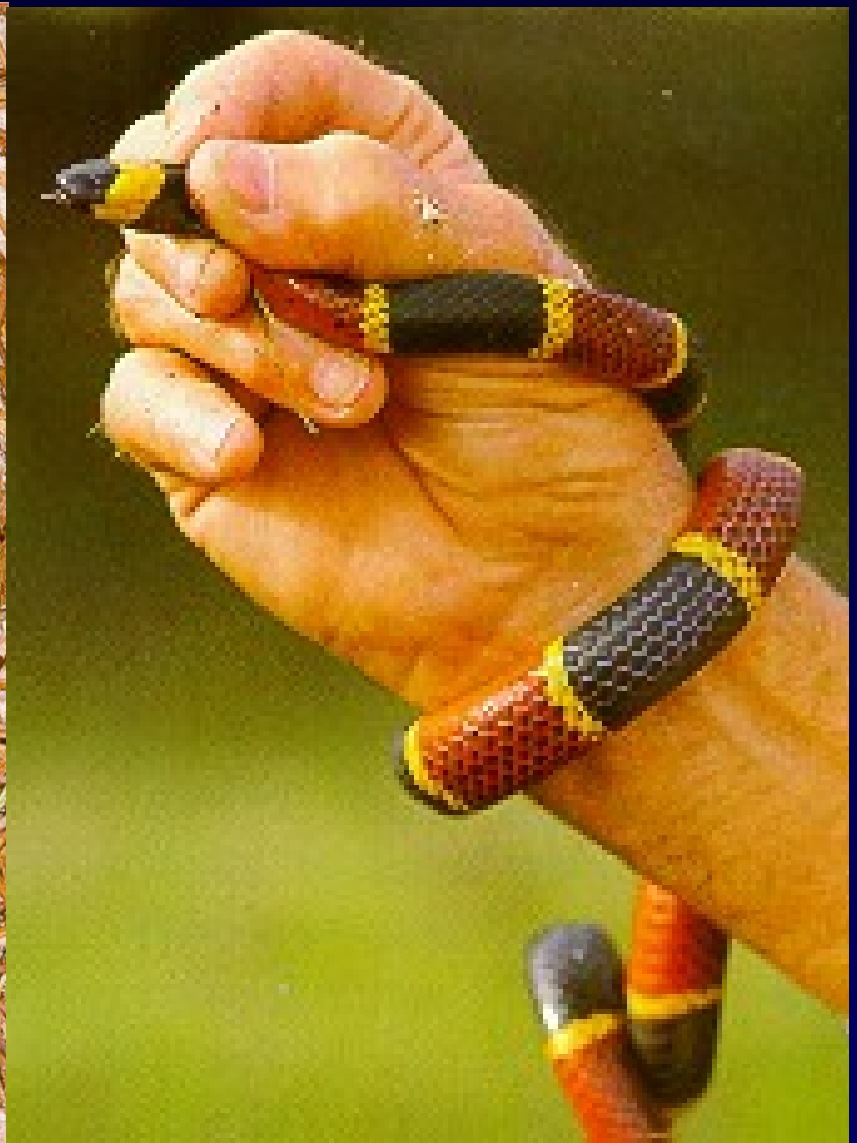
Cottonmouth / water mocassin

Agkistrodon piscivorous

Cottonmouth / water mocassin



Coral Snake



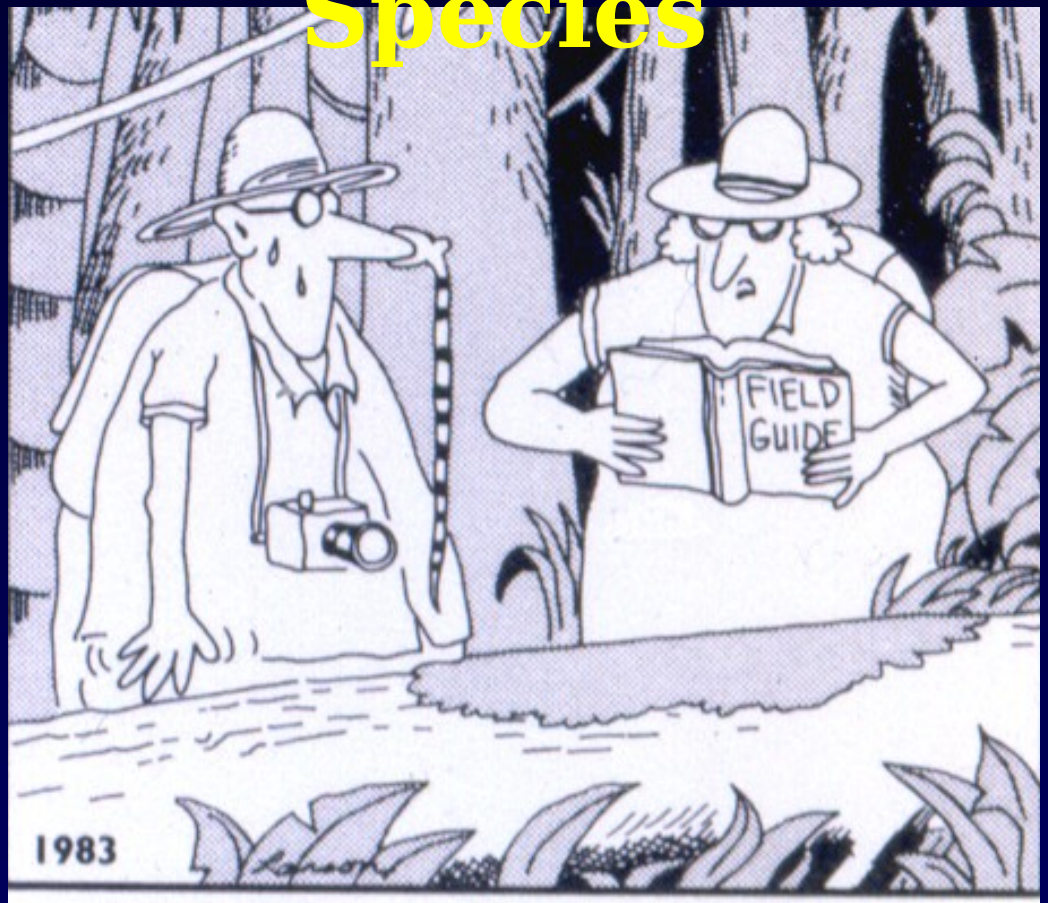
Venomous Snakes
South America and West Indies

- The Caribbean Islands, with the exception of Martinique, St. Lucia, and Trinidad and Tobago, have no venomous snakes.
- South America and the islands with venomous snakes have only *Crotalinae* and *Elapidae*.
- Dangerous Amazonian snakes include:
  - *Crotalinae*: *Bothrops atrox* (barba amarilla), *Bothrops bilineatus* (Amazon tree viper), *Crotalus durisus* (cascabel), *Lachesis mutus* (bushmaster)
  - *Elipadae*: *Leptomicrurus collaris* (slender coral snake), *Micrurus hemprichii* (Hemprich's coral snake), *M. lemniscatus*, *M. psyches*, *M. spixii* (Amazonian coral snake), *M. surinamensis*

Cascabel (*Crotalus durissus*)

Cascabel bite, Guyana, S.

Identification of Dangerous Species



" 'This dangerous viper, known for its peculiar habit of tenaciously hanging from one's nose, is vividly colored.' Oo! Murray! Look! … Here's a picture of it!"

Identification of Dangerous Species
Habitat

- Can be helpful as there are distinct ranges for most species
  - i.e. no cobras in Kansas and no rattlesnakes in Africa
- Can be more difficult in the tropics
  - larger number of species
  - unidentified or poorly studied species
- Attempt to determine indigenous snakes in an area prior to arrival

Identification of Dangerous Species

- Killed snake most useful for identification
  - Only if safely done
- Dead snakes/severed heads can still bite!

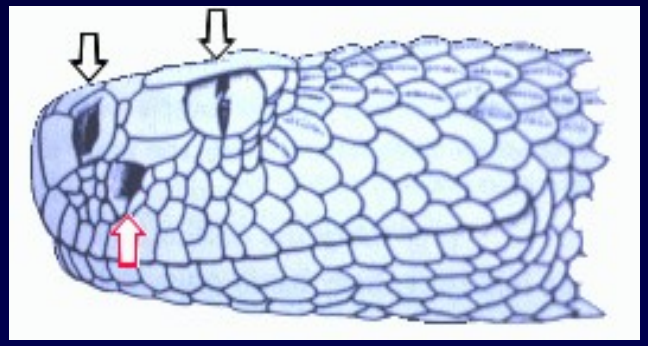
Identification of Dangerous Species
Color and Pattern

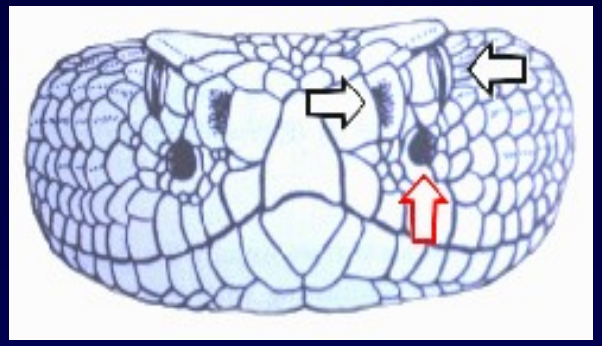
- Widely used, but deceptive
- Real or apparent mimicry of the appearance and behavior by harmless snakes is common
- “Red to black, venom lack; Red to yellow, kill a fellow”
  - Only holds for snakes in U.S., not Mexico, or Central and South America

Identification of Dangerous Species
Head Characteristics

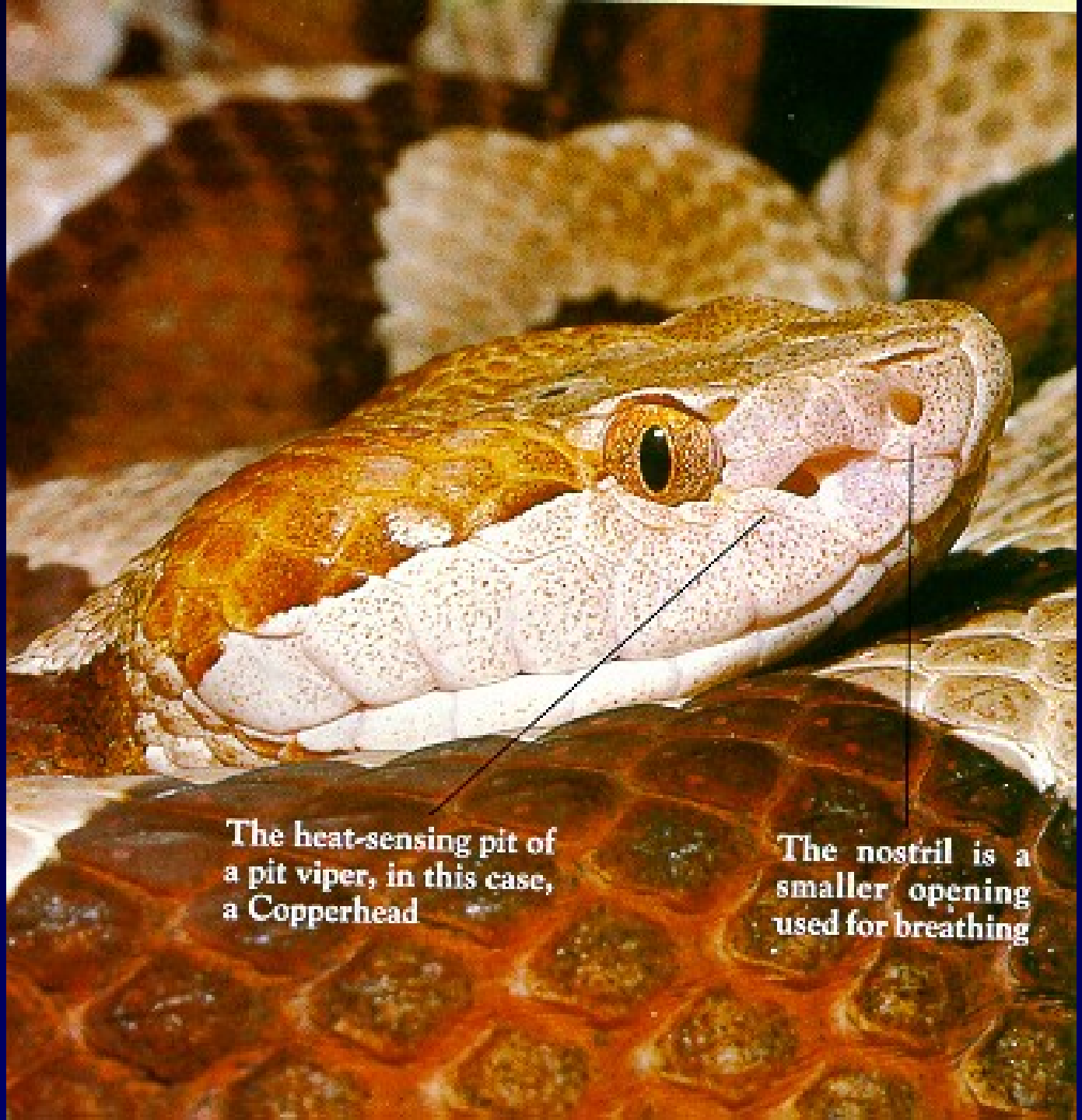
- Presence of facial pits
  - Depressions located below eye and nostril
  - Heat-sensing receptors for prey detection
- Triangular shaped head

Pit Vipers



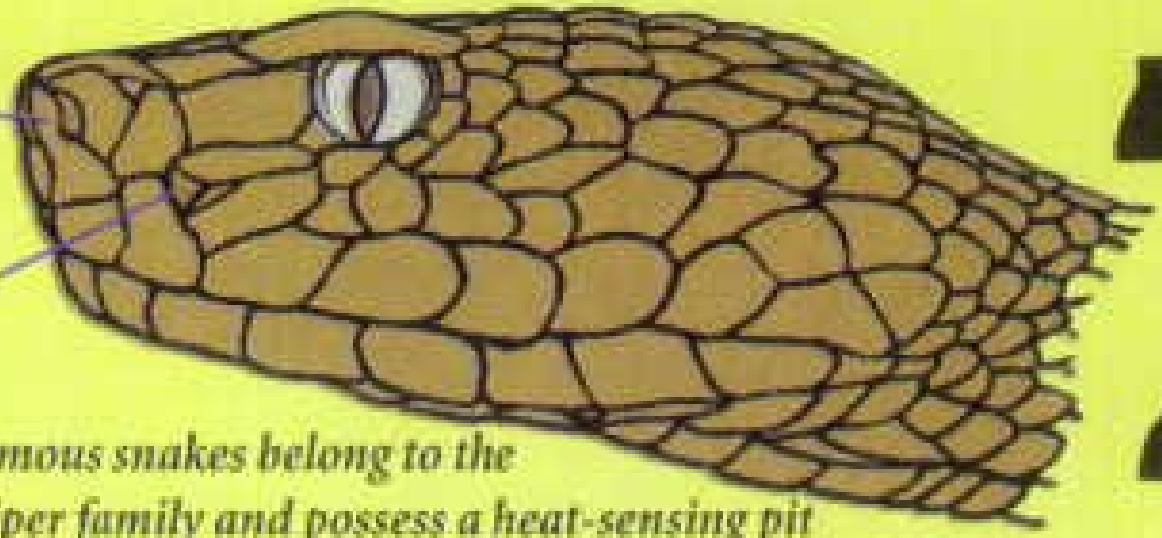


The loreal pit is characteristic of the pit vipers (Family Crotalidae)


The heat-sensing pit of a pit viper, in this case, a Copperhead
The nostril is a smaller opening used for breathing

Identification of Dangerous Species
Eye Characteristics

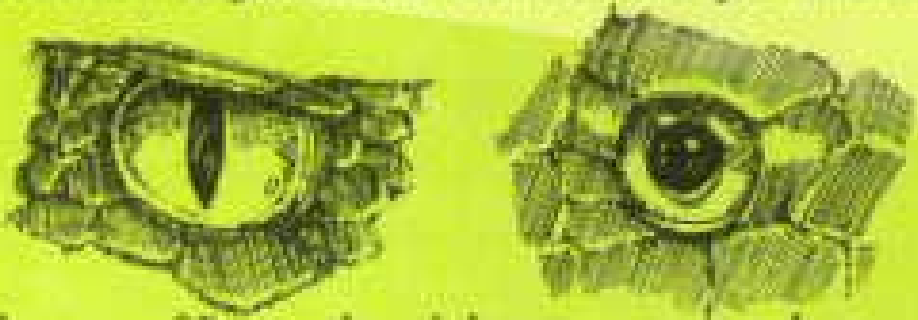
- **Shape of pupil**
  - **– noted in live or freshly killed snakes**
- **Vertical elliptical pupils (“cat’s eye”)**
  - **– most vipers**
- **Round pupils – most venomous elapids**



Venomous

Nonvenomous

Venomous snakes belong to the pit viper family and possess a heat-sensing pit on each side of the head between the eye and nostril.



The eyes of Pennsylvania's venomous snakes have vertical, elliptical pupils resembling those of a cat. Nonvenomous snakes have round pupils like a human eye.

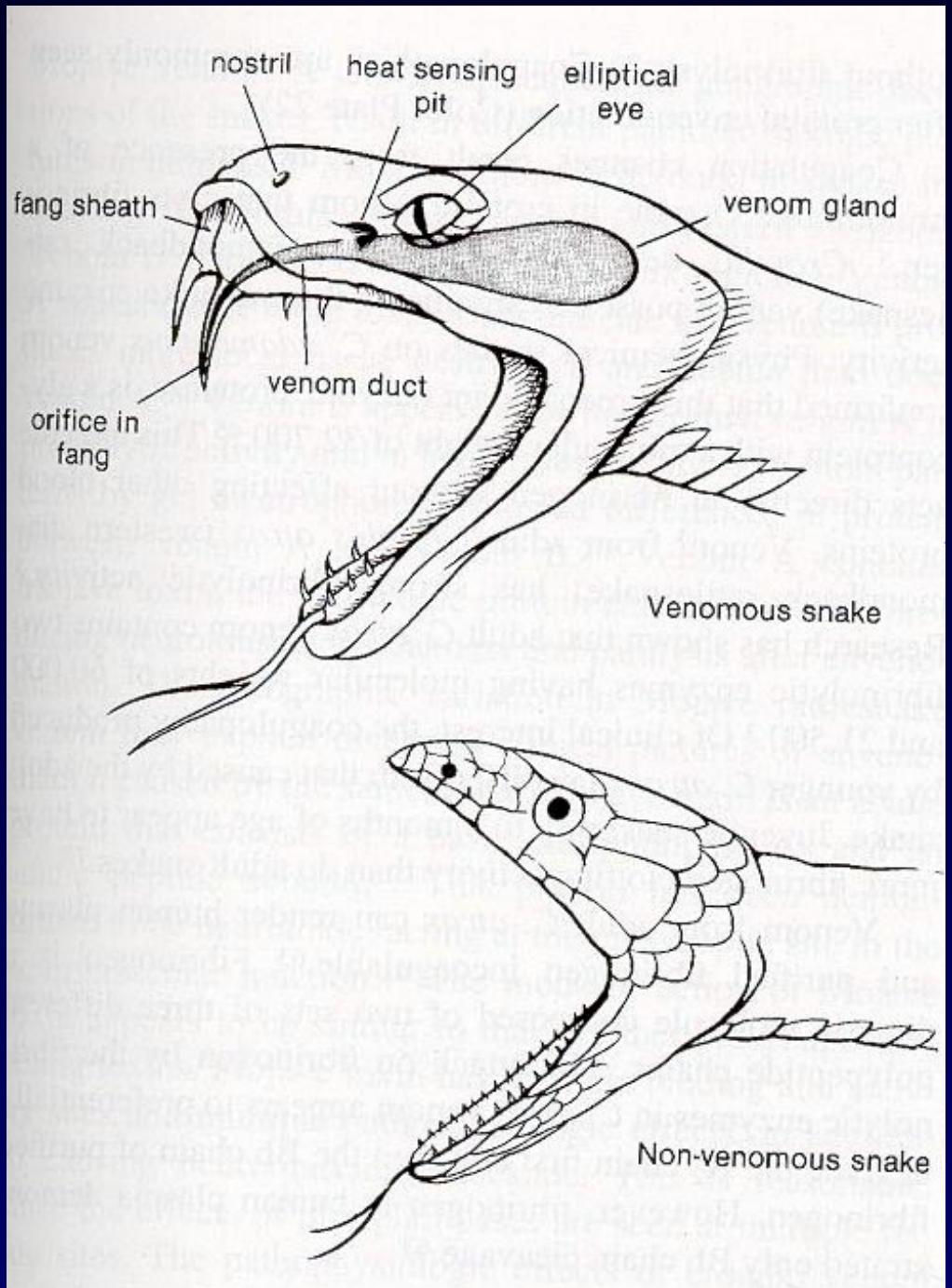
Venomous with rattle

Venomous-scales in single row

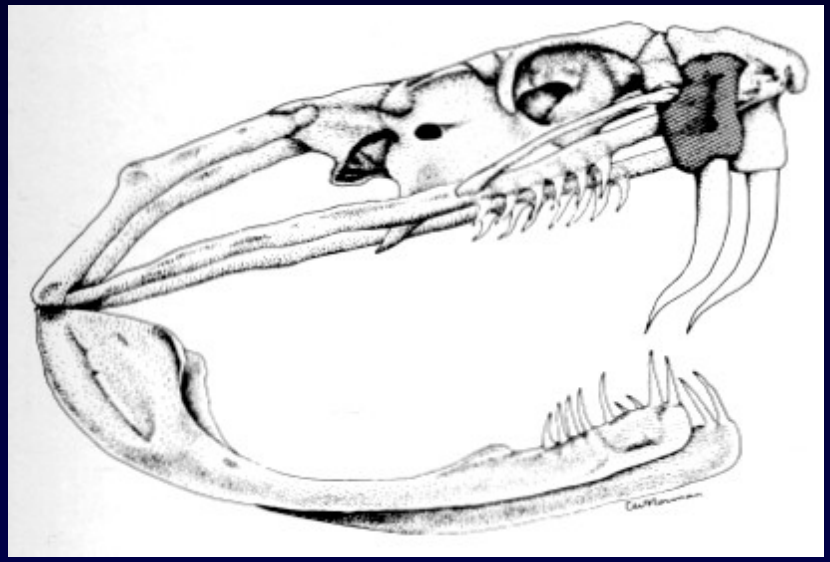
Nonvenomous-scales in double ro

Identification of Dangerous Species
Venom Apparatus / Teeth

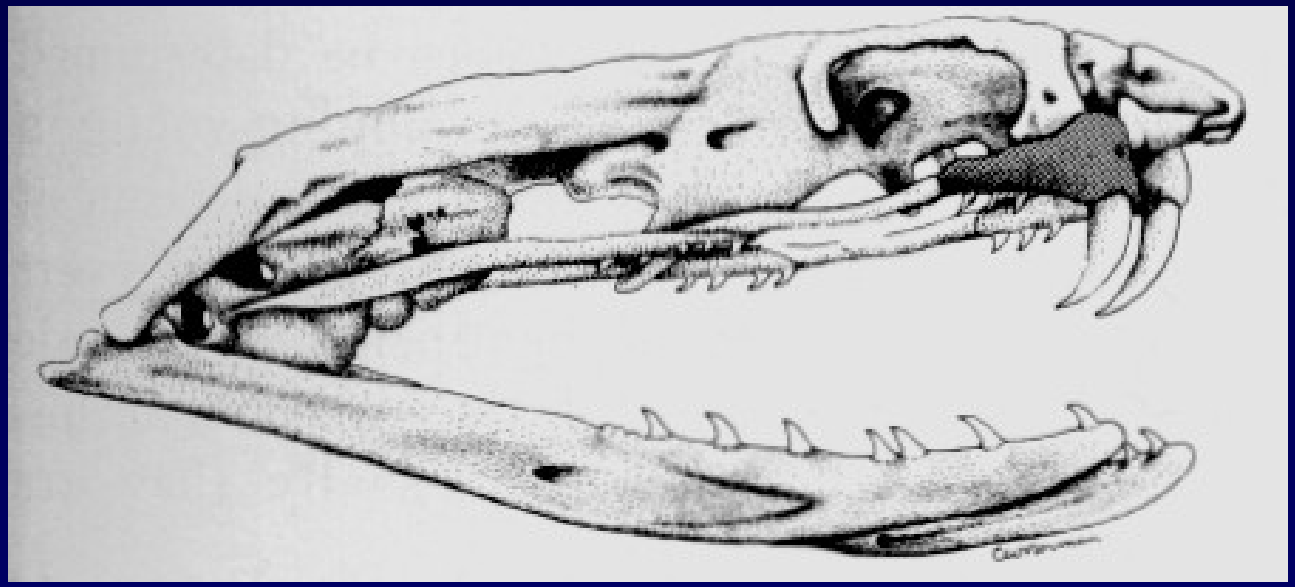
- CAUTION!!
- Vipers: Long, moveable fangs that rotate parallel to roof of mouth, often sheathed in whitish membrane
- Elapids: Fangs are smaller, fixed to the jaw, and located in front of mouth
- Enlarged anterior teeth may also be seen in some nonpoisonous snakes


nostril
heat sensing pit
elliptical eye
fang sheath
venom gland
venom duct
orifice in fang
Venomous snake
Non-venomous snake

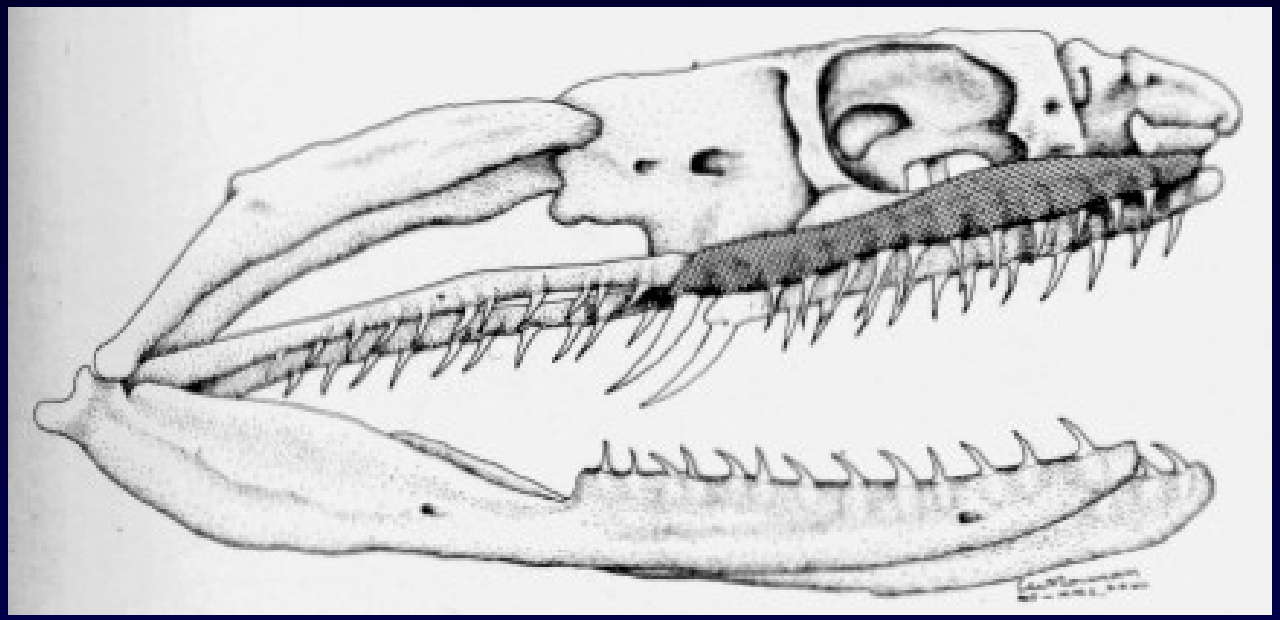
Viperidae Skull



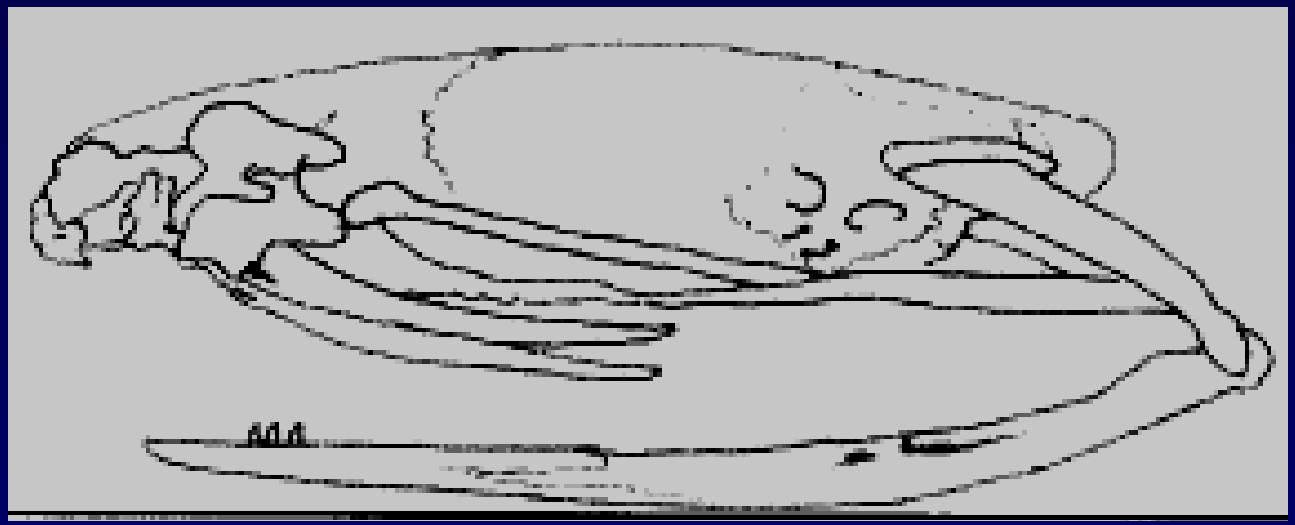
Elapidae Skull



Colubridae Skull



Atractispidae Skull



Snakebite Location

- **Upper extremity: 58%**
  - **especially fingers (up to 20% in some series)**
- **Lower extremity: 38%**
- **Other: 4%**

Snakebite Envenomation

- Most snakes throughout the world are not poisonous
  - Many nonpoisonous snakes also bite
- Bitten but not envenomated
  - Venom not always injected (“dry bite”)
  - Venom may not enter the wound
  - 3 to 40% of bites no signs or symptoms occur

Snakebite
Clinical Features

FAMILY	Envenomated	Time to Death
Elapidae (cobras, kraits)	50%	5 - 20 hours
Hydrophidae (seasnakes)	80%	15 hours
Viperidae (*Crotaline* pit vipers)	30%	2 days

Snakebite – Venom

- **Marked variability in toxicity/composition**
  - **Young and old snakes of same species**
  - **Same species in different areas**
  - **Seasonal variation**
  - **Individual variation**

Snakebite – Venom

- **Complex substances with varying degrees of:**
  - **Numerous different enzymes**
  - **Polypeptide toxins**
  - **Glycoproteins**
  - **Low molecular weight substances**

Snakebite – Pathology

Local Necrosis

- **Tissue effects**
- **Necrosis 2^{o} to hypoxia and direct cellular damage**
- **First aid gone awry**
- **Cold injury**

Envenomation – Local Symptoms

- **Fang punctures:**
  - **May be 1,2, or more**
  - **Superficial lacerations usually do not cause envenomation because venom orifice is above the tip of the tooth**

- **Pain:**
  - **Moderate to severe in 90% of pit viper envenomations**
  - **Sharp, burning pain usually within 5 minutes of the bite**
  - **If no pain within one hour, probably no venom**

- **Edema and erythema**
  - **Characteristic of pit vipers**
  - **Usually within 30 minutes of the bite**
  - **Spread proximal and distal for 12-24 hours**
  - **If not seen within four hours, probably no venom**

Envenomation – *Crotalinae*

Grade	Degree	Clinical Exam/Findings
0	None	Fang marks and min. pain, <1 inch edema
I	Minimal	Fang marks, pain, 1-5 inches edema & erythema in 1st 12 hours
II	Moderate	Fang marks, pain, 6-12 inches edema & erythema in 1st 12 hours, ± systemic symptoms
III	Severe	Fang marks, pain, >12 inches edema & erythema in 24 hours, systemic symptoms and coagulation abnl.
IV	Very Severe	Rapid edema and erythema, ipsilateral ecchymoses, blebs, CV, coag, and renal abln.

Envenomation – *Elapidae*

- **Coral snake envenomations markedly different from pit vipers**
- **Little or no pain/edema up to 5 hours after the bite**
- **Neurologic effects more prominent**
  - **ptosis, dysphagia, dysarthria, hypersalivation**
  - **Loss of DTRs and respiratory depression**

Envenomation – *Elapidae*

Grade	Degree	Clinical Exam/Findings
0	None	Fang scratches or punctures, minor local swelling, no systemic symptoms within 24 hrs of bite
I	Moderate	Fang punctures, minor local swelling, systemic symptoms, respiration may be compromised (but not complete paralysis) within 36 hrs of bite
II	Severe	Grade I with complete respiratory paralysis within 36 hrs of bite

Envenomations – General Symptoms

Crotalids

Sudden symptoms
symptoms
Pain
Edema
Ecchymoses
Vomiting
Weakness
Paresthesias
Tachycardia
Metallic taste
Fasciculations
Oral paresthesias
Confusion
Bleeding
Necrosis
Confusion
Bleeding
Necrosis

Elapids

Delayed onset

Mild pain/painless
minimal to no edema
Nausea
Vomiting
Weakness
Paresthesias
Diplopia
Dysphagia
Fasiculations
Ptosis
Salivation
Diaphoresis
Hyporeflexia
Dyspnea
Confusion
Paralysis
Respiratory

Envenomation – Difficulties

- **Snake bite victims may demonstrate anxiety and hyperventilation**
  - **Resulting in generalized weakness and paresthesias similar to an envenomation**

- **Careful evaluation is required as the patient may not require antivenin, but may need diazepam**

Snakebite Evaluation History

- Time of bite
- Snake description
- Field therapy performed
- PMHx, allergies, horse or sheep exposure, previous horse/sheep serum or bites

Snakebite Evaluation Physical

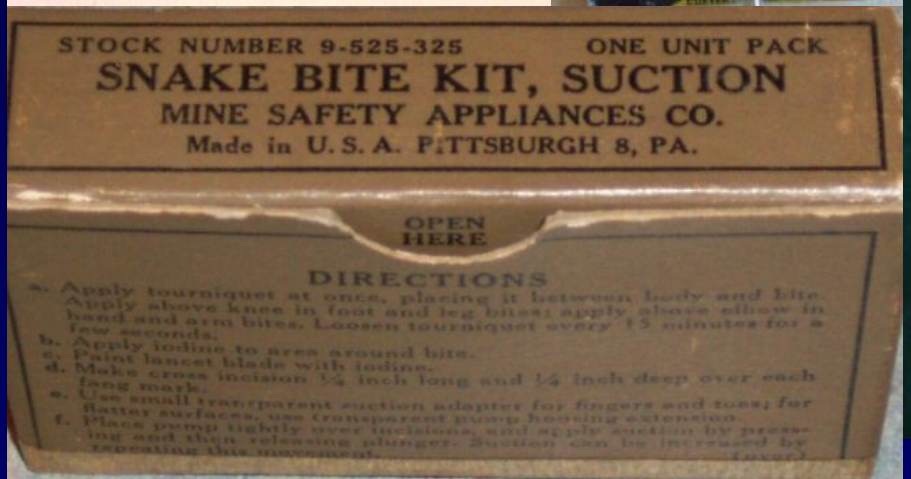
- **Tooth marks / Fangs**
  - **may be multiple bites and envenomations**
- **Baseline vitals**
- **Neurological status**
- **Circumferential measurement of affected limb**
- **Do not remove tourniquet until patient monitored**
  - **Be prepared to treat for respiratory arrest and shock**

Snakebite – Laboratory Evaluation

- **Any degree of envenomation**
  - **Type and cross (before antivenin given)**
  - **CBC**
  - **PT, PTT, fibrinogen**
  - **BUN/Cr, glucose**
  - **Urinalysis**

- **Severe envenomation**
  - **Serial electrolytes**
  - **Serial coags**
  - **EKG (pts over 40yo or presenting with CV abnormality)**

Snakebite Treatment and First Aid Measures



Snakebite Evaluation
General Treatment

Treating all snakebites the same would be similar to treating all infections the same

- **Two large-bore IVs**
- **Tetanus toxoid after wound cleaning and debridement**

Snakebite Treatment

- Recommendations for “field treatment”?
- First Aid importance often exaggerated
- Medical treatment at hospital is crucial for envenomations

First Aid

- Reassure patient
- Immobilize affected limb
- Remove items that may cause constriction
- Transport ASAP
- Avoid doing harm

First Aid – Incision and Suction

Rationale: to remove venom and decrease envenomation

- Superficial incision through fang marks
  - Fangs are curved; venom may be deposited below marks
  - Creates unsterile, poorly healing wounds
  - May damage underlying structures
  - Oral suction may envenomate as well as introduce mouth flora into the wound

- If suction can be performed by a trained person within 5 minutes of the bite, it may be beneficial

- Suction devices (Sawyer extractor) efficacy?
  - Unlikely to cause additional injury and can be used quickly

First Aid – Cryotherapy

Rationale: to decrease edema and inactivate venom

- Does not reduce envenomation-associated edema
- Cold-induced vasoconstriction prevents antivenin penetration
- Does not inactivate venom; local vasoconstriction increases vulnerability of compromised tissue
- Of 36 bites leading to amputation, 75% had prior cryotherapy
- Probably safe if ice is used as a pack for pain control for short periods of time

First Aid – Ligatures

- **Rationale:** to impede systemic spread of venom
- Inappropriately applied tourniquets
  - If left for long periods can lead to ↑ tissue necrosis
- Lymphatic constriction efficacy?
  - If greater than 30 min from medical care, may be beneficial if applied by a trained person

First Aid – Immobilization

- **Rationale:** to reduce movement of venom from the limb to circulation
- Movement of the affected limb does increase movement of venom into the circulation
- **Splint as if the limb were fractured and keep below the level of the heart.** If possible do not allow to walk.
- Pressure dressing applied over fang site
  - recommended by some Australians, but not universally accepted

Snakebite – Supportive Care for Neurotoxin

- Especially cobras, kraits, and coral snakes, but also for serious rattlesnake envenomations

- Intubate and ventilate
  - No pathologic lung changes
  - Damage is completely reversible

- Avoid aspiration
  - Nausea and vomiting are frequently seen effects of venom
  - Position patient on side
  - Frequent suctioning

Snakebite – Antivenin

- **In the U.S. there are three main products**
  - **two crotalinae (ACP, CroFab)**
  - **one elapidae**

Antivenin *Crotalidae* polyvalent (ACP)

- **Pit viper antivenin from Wyeth-Ayerst polyvalent North and South American antisnake serum from immunized horses**
  - **Four species of pit vipers used: Eastern and Western Diamondback Rattlesnakes, Tropical Rattlesnake, and the Fer de Lance**
  - **Due to antigenic similarity, can be used for all North American rattlesnakes, pygmy rattlesnakes, copperheads, cottonmouths, South and Central American *Bothrops* sp. (Fer de Lance) and bushmaster**

Antivenin *Crotalidae* Polyvalent Immune Fab (CroFab)

- **Purified immunoglobulin fragment from sheep immunized with:**
  - **Western and Eastern Diamondback Rattlesnakes**
  - **Mojave Rattlesnake**
  - **Cottonmouth**

- **Shorter $t_{1/2}$ (12-24hr vs. 61-194hr for equine)**
- **More effective in animal studies in preventing death**
- **Severe envenomations in human studies showed resolution of thrombocytopenia within 1 hour after treatment**
- **Rash, urticaria, and pruritus in 1/3 but ? less anaphylaxis and serum sickness**
- **Expensive (12 vials - $9300)**
  - **Should be refrigerated, but safe after 60 days at 120°F and no loss in potency until 160°F for at least 30 days**

Antivenin – Elapids

- ***Micrurus*** **(coral snake) antivenin**
  - **good for all North American (and most South American) coral snakes**
  - **except the Arizona coral snake**

- **Australia, Asia, and South American countries produce antivenins for local elapids that are more specific than those produced in the U.S.**

Antivenin Indications

- **Edema of greater than one half of the bitten extremity**
- **Systemic signs**
  - **Spontaneous bleeding from sites distant to the wound**
  - **Signs of CV involvement**
    - **dysrhythmias, drop in BP, EKG abnormalities**
  - **Renal dysfunction**
    - **oliguria, hematuria, rising creatinine**

Antivenin Contraindications

- No absolute contraindications
- If known hypersensitivity to equine serum
  - Judgement must be made whether to use or not
  - Desensitization can be performed
  - Ovine antivenin (CroFab) can be used
- Not using in severe envenomation may result in loss of limb or death

Antivenin Timing

- **If patient has a tourniquet, attempt to administer antivenin prior to its release**

- **Most effective when administered within four hours of the bite**
  - **Can be given after 24hrs in severe cases**
  - **Probably some effect even a week later**

Antivenin – Skin Testing

- **Routine skin testing??**
- **Patients should be in monitored bed with preparation to treat for anaphylaxis**
- **0.02 ml of diluted (1:10) horse serum ID in one arm and the same volume of normal saline in the other arm (if allergic to horse serum then use 1:100 dilution)**
- **1% of individuals with negative skin test will have some reaction**

Antivenin – Dosing Guidelines ACP

Degree of envenomation	Antivenin Dose ACP
None	None required
Minimal	2-4 vials
Moderate	5-9 vials
Severe	10-15 vials

- Per Wyeth package insert: dose→reassess→dose→reasess
- Same dose in adults and children (some recommend 1.5-2x higher in children)
- Administer dose over 30 min to 2 hours. Repeat dose if no improvement after 1-2 hrs until pain, edema, and systemic reactions have resolved

Antivenin – Dosing Guidelines Fab AV

- **Large dose to achieve initial control (i.e. cessation of venom components)**
  - **Local effects**
  - **Systemic effects**
  - **Coagulopathy**
- **Start with 3-12 vials**
  - **Additional vials given at 6, 12, and 18 hrs**
  - **Thrombocytopenia and coagulopathy may return if additional doses are not used**
- **Initial dose diluted to 250ml and given IV over 1 hour**
  - **Slowly for 1st ten minutes and then remainder completed in 1 hr**

Antivenin – Administration

- **Observe**
- **Be ready to treat for anaphylaxis**
  - **Epinephrine, diphenhydramine, steroids**
  - **Intubation equipment at bedside**
  - **Cardiac monitor**

Antivenin – Monitoring Response

- End of spontaneous bleeding
  - Normalization of coags takes longer, may follow whole blood clotting time at bedside
- Clearing of hemoglobinuria/myoglobinuria
- Return of EKG and BP to normal
- Decrease in ptosis and other paralytic signs
  - Increased tidal volume
  - Increased maintenance of upward gaze

Antivenin – Reactions to ACP

- **Early**
  - **Mild 2-20% easily treatable**
  - **Death – rare; < 1 in 5,000 (may have been due to venom)**
    - **Rx epinephrine, diphenhydramine, steroids**
  - **Prediction of reactions: skin tests unreliable and may lead to anaphylaxis themselves**

- **Late**
  - **Serum sickness from horse serum**
    - **Occurs 5-24 days after dose**
    - **Up to 75% of patients**
    - **Rx diphenhydramine and steroids**

Snakebite – Surgery

- **Careful, prompt surgical management is crucial to minimize damage in necrotic cases**

- **Fasciotomy not necessary in most cases**
  - **Only use if increased tissue pressure or severe narrowing of a major vessel by objective evidence (i.e. doppler or angiography)**

References

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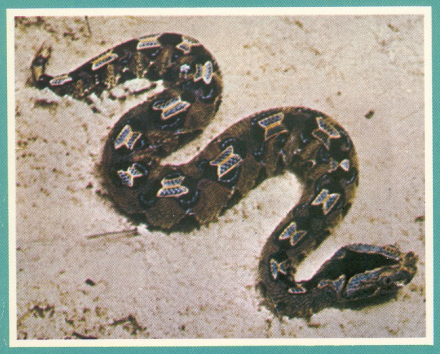
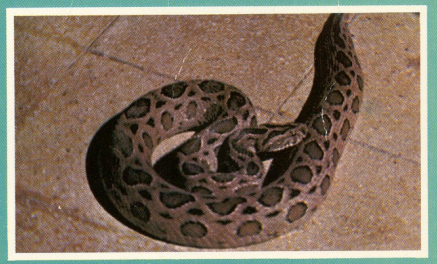
POISONOUS SNAKES OF THE WORLD

U.S. Department of the Navy
(Bureau of Medicine and Surgery)





King Cobr

Spitting Cobra

Black Mamba (*Dendroaspis polylepis*)

Okinawa Habu

Fer de lance

Gaboon Viper

Krait

FIGURE 4. Puff Adder, *Bitis arietans* (VIPERIDAE). Photo by J. Markham. (See